

Living with LUNG CANCER

▶ The disease that used to be a death sentence isn't necessarily so anymore. Some women are managing it—and even thriving. BY Leslie Goldman

WHEN LINNEA OLSON was told in June 2008 that the cancer she'd been battling for three years had spread from one lung to the other, she began preparing to die.

Given just three to five months to live, the then-48-year-old artist and lifelong nonsmoker embarked on a "farewell tour," saying goodbye to family and friends and arranging grief counseling for her youngest son (then 11). She wasn't sure she'd live long enough to make it to her daughter's wedding later that summer; when she did, she spent the day looking at her three children and thinking about how their lives would be after she was gone.

Then an oncologist tested Olson's cancerous tissue for a specific genetic mutation whose presence enabled Olson to enroll in a clinical trial for a drug called crizotinib (brand name Xalkori). What happened next seemed nothing short of miraculous. "Within days, my constant coughing and shortness of breath were gone," Olson says. Seven weeks later, every single one of the 33 tumors in her lungs had almost completely disappeared.

As recently as 20 years ago, a turnaround like this would have been unheard of. And indeed, according to the American Cancer Society, lung cancer still kills more women than breast, ovarian, and uterine cancers combined, with a five-year survival rate of only 21 percent. Yet despite the disease's ferocious nature, the medical community's understanding of it has recently evolved—with the result that some patients are outliving dire prognoses and many more are filled with hope.

Olson, like up to 15 percent of Americans diagnosed with lung cancer, is a "never-smoker"—medical-speak for those who have smoked fewer than 100 cigarettes in their lifetime. Though exposure to air pollution, radon, and secondhand smoke are risk factors, science doesn't yet know all the reasons why such patients are being diagnosed in increasing numbers, says Andrea McKee, MD, chairman of radiation oncology for Lahey Hospital & Medical Center in Massachusetts and a scientific adviser for the American Lung Association. Still, oncologists are learning more every day. "We're discovering how lung cancer behaves, how the cells differ between nonsmokers and smokers, and how we can use various genetic mutations to shape treatment," McKee says.

One game-changing finding is what led to Olson's reprieve: About 50 to 60 percent of never-smoking patients have one of many targetable mutations in their lung cancer cells that cause the cells to multiply and divide more quickly and aggressively, explains Olson's oncologist, Alice Shaw, MD, PhD, director of thoracic oncology at Massachusetts General Hospital. (By comparison, about 20 percent of all lung cancer patients, regardless of smoking history, are thought to have such driver mutations. Women seem to be slightly more prone to them than men.) Over the past five years, Shaw says, it's become standard practice for patients diagnosed with advanced lung cancer to have their tumors tested for these mutations, called oncogenes, which cause cancer when activated.

Why does that matter? "Now that we have a better understanding of what is driving these cancers' growth," says Shaw, "it opens up a whole new array of treatment options." Among them: targeted therapies, including tyrosine kinase inhibitors (TKIs), the first of which were approved by the Food and Drug Administration for treating some lung cancers in 2003. TKIs have kept Olson thriving for years past her original prognosis.

Easier to tolerate than traditional chemotherapy, which notoriously attacks even healthy cells in a patient's body in an effort to kill the cancerous ones, TKIs are oral medications that home in on cancer cells specifically, turning off oncogene mutations. Because of this selective assault, fewer healthy cells are affected, and side effects can be milder than with chemotherapy (although TKIs can still cause nausea, diarrhea, memory problems, and fatigue—which Olson has experienced). Patients take a pill once or twice daily and undergo tests every few months to monitor progress. In clinical trials, up to 90 percent of patients with certain mutations experience some degree of tumor shrinkage or stabilization, extending life expectancy. The catch is that in all likelihood, the cancer



As many as 20 percent of Americans who die from lung cancer have never smoked.



will eventually become resistant to the drug, typically after a year or two, which means patients will need to try a different treatment. Olson is on her third TKI.

Targeted therapies aren't the only new life-extending option. When lung cancer patients are screened for oncogene mutations, they're also tested for something called PD-L1 expression; here, doctors are looking for a critical mass of tumor cells that produce a high amount of a particular protein marker. "If the PD-L1 results are high enough, and the other actionable mutations are not present, then you try immunotherapy," says Patricia L. Rich, MD, medical oncology director of Cancer Treatment Centers of America's Lung Cancer Institute.

That's what happened in Nancy Vandespool's case.

Vandespool, a 47-year-old New Yorker, beat stage III lung cancer in 2012 via chemotherapy, radiation, and surgery. Then, in 2016, the never-smoker was horrified to learn her cancer had returned. Her doctors tested her growing tumor, hoping it might respond to drugs that harness the immune system to fight cancer.

"Cancer cells are smart—smart enough to release chemical signals that tell the immune system to stop fighting them," explains Rich. "But immunotherapy treatments can turn off those signals or help the body generate supercharged cancer-killing immune cells." Currently approved for advanced lung cancers as well as melanoma and cancers of the head and neck, kidneys, and a few others, immunotherapy typically involves an IV infusion every two to three weeks. Never-smokers have seen benefits.

So far, the results are impressive: A *New England Journal of Medicine* study found that for patients who'd already had a round of chemotherapy, the overall survival rate at one year was 42 percent for those on the immunotherapy drug nivolumab (Opdivo), versus 24 percent for just a second round of chemo. Combining the two is even more promising: Patients using the immunotherapy drug pembrolizumab (Keytruda) plus chemo had an overall response rate of 55 percent compared with 29 percent for chemo alone. However, as with targeted therapy, patients are likely to develop a resistance that will necessitate switching to another drug.

Immunotherapy seemed to stop Vandespool's tumor in its tracks: It didn't grow or spread in the year since her last treatment in January 2017. She doesn't talk about her prognosis with her physicians; she's focusing on "enjoying every breath I take." The side effects of immunotherapy—fatigue, nausea, and ever-present full-body pain—have had an impact on Vandespool's day-to-day life. "But at least I *have* a 'rest of my life,'" she says. "I used to be able to chase my grandson around the park; now I sit and watch him play. And I'm so happy to be able to do that and to be able to kiss my family and just be alive." She credits family and friends locally and in Puerto Rico (where she's originally from) for helping keep her spirits up.

Olson, for her part, cheekily calls herself "terminally optimistic." She's living in an artists' community in Lowell, Massachusetts, and spends her time painting, doing street photography, and working on a blog called *Life and Breath: Outliving Lung Cancer*. "I may not be a survivor," she says, "but for now, I am surviving."

Finding Solidarity in Uncertainty

As lung cancer patients outlive traditionally short life expectancies, they face new hurdles, like coping with the stress of frequent scans and the accompanying fear of what they might reveal. Olson calls it OTSD: ongoing traumatic stress disorder. "I feel fabulous," she says, "but the fear of cancer returning is constant. Can I plan a vacation a year from now? Is it worth spending money on dental work? Plus, almost a third of my income goes to healthcare."

The constant ups and downs make social support essential, McKee says: Studies show patients without a support network have poorer overall survival rates.

For Vandespool, emotional sustenance has come from immersing herself in the American Lung Association's Lung Force initiative, a female-centric awareness-raising effort that she credits with introducing her to the concept of immunotherapy. "We do fundraising walks, we've lobbied Congress to finance more research, and I've met other women like myself who have become part of my family."